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Macromineral physiology and application to the feeding of the dairy cow for prevention of milk fever and other periparturient mineral disorders☆

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Abstract

The periparturient cow undergoes a transition from non-lactating to lactating at calving. The animal is tremendously challenged to maintain calcium homeostasis. Those that fail can develop milk fever, a clinical disorder that is life threatening to the cow and predisposes the cow to a variety of other disorders. Less dramatic sub-clinical hypocalcemia can also reduce productivity of cattle by reducing feed intake in early lactation. The cause and prevention of milk fever will be discussed, focusing on the role of diet cation–anion difference and use of low calcium diets. The periparturient period also typically causes minor perturbations in blood potassium and phosphorus concentrations. Occasionally these disturbances are severe enough to be the cause of recumbency and the "downer cow" syndrome. Pathogenesis of these syndromes will be discussed. Low blood magnesium concentrations are observed when animals are fed inadequate amounts of magnesium or some factor is present in the diet, which prevents adequate absorption of magnesium. Severe hypomagnesemia can cause tetany and the downer cow syndrome, but more commonly moderate hypomagnesemia impairs the ability of the cow to maintain calcium homeostasis and hypocalcemia occurs secondary to the hypomagnesemia.
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1. Introduction

Inadequate blood calcium (Ca), phosphorus (P), magnesium (Mg), or potassium (K) concentrations can cause a cow to lose the ability to rise to her feet as these minerals are necessary for nerve and muscle function and are therefore of particular concern in the newly calved cow. Less severe disturbances in blood concentrations of these minerals can cause reduced feed intake, poor rumen and intestine motility, poor productivity, and increased susceptibility to other metabolic and infectious disease. Mechanisms for maintaining blood Ca, P, Mg and K concentrations perform efficiently most of the time but occasionally these homeostatic mechanisms fail and metabolic diseases such as milk fever occur. Understanding how and why these mechanisms fail may allow the practitioner to develop strategies to avoid these disorders.

2. Calcium

2.1. Ca Homeostasis

Blood Ca in the adult cow is maintained around 2.1–2.5 mmol/L. In order to prevent blood Ca from decreasing at the onset of lactation, which has a variety of severe consequences to life processes beyond parturient paresis, the cow must replace Ca lost to milk by withdrawing Ca from bone or by increasing the absorption of dietary Ca. While this is potentially damaging to bones (lactational osteoporosis typically results in loss of 0.09–0.13 of skeletal Ca in dairy cows, which is reversible in later lactation), the main objective – to maintain normocalcemia – can be achieved. Bone Ca mobilization is regulated by parathyroid hormone (PTH), which is produced whenever there is a decline in blood Ca. Renal tubular reabsorption of Ca is also enhanced by PTH. However, the total amount of Ca that can be recovered by reducing urinary Ca excretion is relatively small. A second hormone, 1,25-dihydroxyvitamin D, is required to stimulate the intestine to efficiently absorb dietary Ca. This hormone is made within the kidney from Vitamin D in response to an increase in blood PTH. Put simply, hypocalcemia and milk fever occur when cattle do not extract enough Ca from their bones and diet to replace the Ca lost to milk. Several nutritional factors are involved in the breakdown of Ca homeostasis that results in milk fever.

3. Factors impairing Ca homeostasis at the cellular level

3.1. Metabolic alkalosis

Metabolic alkalosis predisposes cows to milk fever and subclinical hypocalcemia (Craige and Stoll, 1947). Metabolic alkalosis blunts the response of the cow to PTH (Gaynor et al., 1989; Goff et al., 1991; Phillippo et al., 1994). *In vitro* studies suggest the conformation of the PTH receptor is altered during metabolic alkalosis rendering the tissues less sensitive to PTH (Martin et al., 1980; Bushinsky, 1996). Lack of PTH responsiveness by bone tissue prevents effective utilization of bone canaliculi fluid Ca, sometimes referred to as osteocytic

osteolysis, and prevents activation of osteoclastic bone resorption. Failure of the kidneys to respond to PTH reduces renal reabsorption of Ca from the glomerular filtrate. More importantly, the kidneys fail to convert 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D. Therefore, enhanced intestinal absorption of dietary Ca that normally would help restore blood Ca to normal, fails to be instituted. Metabolic alkalosis is largely the result of a diet that supplies more cations (K, sodium (Na), Ca, and Mg) than anions (chloride (Cl), sulfate (SO_4), and phosphate (PO_4)) to the blood. In simplest terms, a disparity in electrical charge in body fluids occurs in animals fed these diets because a greater number of positively charged cations enter the blood than negatively charged anions. To restore electroneutrality to this positively charged blood, a positive charge in the form of a hydrogen ion (H^+) is lost from the blood compartment and the pH of the blood is increased (Stewart, 1983). For a more detailed description of how dietary cation–anion balance influences blood pH, the reader is referred to recent reviews on this subject Constable (1999) and Goff (2000). Adding readily absorbable anions to the diet increases the total negative charges in the blood allowing more H^+ to exist and the blood pH decreases.

3.2. Hypomagnesemia

Hypomagnesemia affects Ca metabolism in two ways: (1) by reducing PTH secretion in response to hypocalcemia and (2) by reducing tissue sensitivity to PTH. PTH secretion is normally increased greatly in response to even slight decreases in blood Ca concentration. However, hypomagnesemia can blunt this response (Rude et al., 1978; Littledike et al., 1983).

The integrity of the interaction between PTH and its receptor is vital to Ca homeostasis. Hypomagnesemia, independent of metabolic alkalosis, can also interfere with the ability of PTH to act on its target tissues. When PTH binds its receptor on bone or kidney tissues, it normally initiates activation of adenylate cyclase, resulting in production of the second messenger, cyclic AMP. PTH–receptor interactions should also cause activation of phospholipase C in some tissues, resulting in production of the second messengers diacylglycerol and inositol 1,4,5-triphosphate. Both adenylate cyclase and phospholipase C have a Mg++ binding site which must be occupied by a Mg ion for full activity (Rude, 1998). In man, it is well recognized that hypomagnesemia can cause hypocalcemia and that Mg therapy alone restores the serum Ca concentration to normal; Ca and/or Vitamin D therapy are ineffective (Rude, 1998). Field evidence suggests that blood Mg concentrations below 0.65 mmol/L in the periparturient cow will increase the susceptibility of cows to hypocalcemia and milk fever (van de Braak et al., 1987).

3.3. Excessive blood phosphorus concentration

When blood P concentration is increased above the upper normal limit, around 2 mmol/L, the phosphate has a direct inhibitory effect on the renal enzyme converting 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D. Therefore, even if PTH secretion occurs and the tissues recognize the PTH the cow will be unable to produce the hormone necessary for activation of intestinal Ca transport and the cow will suffer impaired Ca homeostasis (Barton, 1978; Kichura et al., 1982).

3.4. Strategies to prevent hypocalcemia

3.4.1. Reducing diet cation–anion difference

In theory, all the cations and anions in a diet are capable of exerting an influence on the electrical charge of the blood. The major cations present in feeds and the charge they carry are Na (+1), K (+1), Ca (+2), and Mg (+2). The major anions and their charges found in feeds are Cl (−1), SO_4 (−2), and phosphate (assumed to be −3). Cations or anions present in the diet will only alter the electrical charge of the blood if they are absorbed into the blood. Trace elements present in diets are absorbed in such small amounts that they are of negligible consequence to acid–base status. Organic acids such as the volatile fatty acids are generally absorbed in the undissociated form so that they carry both a positive and negative charge into the blood. They also are rapidly metabolized within the liver so they have only a small effect on general acid–base balance under most circumstances.

The difference between the number of cation and anion particles absorbed from the diet determines the general acid–base balance of the body and therefore, the pH of the blood. The cation–anion difference of a diet is commonly described in terms of mEq/kg DM (some authors prefer to use "mEq/100 g" diet DM) of just Na, K, Cl, and SO_4 (traditionally calculated on S concentration reported when diet is analyzed by wet chemistry) as follows:

$$\text{Dietary cation–anion difference (DCAD)} = (\text{mEq Na}^+ + \text{mEq K}^+) - (\text{mEq Cl}^- + \text{mEq S}^{2-}).$$

This equation is useful, although it must be kept in mind that Ca, Mg, and P absorbed from the diet will also influence blood pH. Evaluation of the relative acidifying activity of dietary Cl *versus* SO_4 demonstrate SO_4 is only about 0.6 as acidifying as Cl (Oetzel et al., 1991; Tucker et al., 1991; Goff et al., 2004). Thus, the DCAD of a diet and its acidifying activity is more accurately expressed by the following equation: $(Na^+ + K^+) - (Cl^- + 0.6\,S^{2-})$. A more complex DCAD equation would include Ca, Mg, and P. It should probably also include ammonium, as this cation seems to contribute to the cation content of the blood as well (Constable, 1999). Unfortunately experimental data are lacking that would allow assignment of a coefficient of absorption to each of these dietary ions when fed to the dry cow. While DCAD equations provide a theoretical basis for dietary manipulation of acid–base status they are not necessary for formulation of mineral content of prepartum dairy cow rations because, with the exception of K and Cl, the rate of inclusion of the other macrominerals can be set at fixed rates.

The USA National Research Council (NRC, 2000) requirement for Na in the diet of a late gestation cow is about 1.2 g/kg DM. Feedstuffs typically used in rations for late gestation cows generally do not supply this amount of Na. (Exceptions occur, especially when forages are grown where irrigation has led to salinity of the soil.) A small amount of salt is added to the diet to prevent pica, which often is manifest as a desire to drink urine from the floor. Unlimited access to NaCl is to be avoided in late gestation because it will increase the risk of udder edema, not because it greatly affects acid–base status.

At least two studies have clearly demonstrated that inclusion of Ca in the diet at NRC required levels or several fold above NRC required levels does not influence the degree of hypocalcemia experienced by the cow at calving (Goff and Horst, 1997; Beede et al.,

2001). Beede et al. (2001) fed 4.7, 9.8, 15.2, and 19.5 g Ca/kg DM to cows in late gestation being fed a high Cl diet to prevent milk fever. Cows fed 15 g Ca/kg DM diets had slightly reduced feed intake when compared to control cows while those fed the 19.5 g Ca/kg DM had significantly lower feed intake. Dietary Ca did not influence the degree of hypocalcemia experienced at calving or milk production in the subsequent lactation. It appears from this study that close-up diet Ca concentration should be maintained between 8.5 and 10 g Ca/kg DM.

To ensure adequate concentrations of Mg in the blood of the periparturient cow so that PTH interacts effectively with its receptors on bone and kidney cells the dietary Mg concentration should be 3.5–4 g Mg/kg DM. This higher dietary Mg concentration allows the cow to take advantage of passive absorption of Mg across the rumen wall, which will be discussed further in Section 3.6.

Dietary P concentration should be fed at a level to meet the NRC requirement for P in the late gestation cow. This is generally about 0.4 g P/kg DM for most cows, though recent studies suggest this may overestimate the true requirement of the cow for dietary P (Peterson and Beede, 2002). A diet supplying more than 80 g P/day (Barton, 1978; Kichura et al., 1982), or utilizing dietary P in the form of phosphoric acid as an anion to acidify the blood of the cow (Crill et al., 1996), will block production of 1,25-dihydroxyvitamin D and cause milk fever.

Dietary S must be kept above 2.2 g/kg DM to ensure adequate substrate for rumen microbial amino acid synthesis. Corn (maize) silage diets are notoriously low in sulfur. Diet S should be kept below 4 g/kg DM to avoid possible neurological problems associated with S toxicity (Gould et al., 1991). This is because sulfate and sulfur entering the rumen can be reduced to sulfide. A portion of the sulfide produced in the rumen is in the form of hydrogen sulfide and enters the gas cap above the rumen liquors. Since ruminants ordinarily inhale rumen gases during eructation (Dougherty and Cook, 1962), hydrogen sulfide in the rumen gas is inhaled and rapidly absorbed which can cause toxicity at dietary levels that would be rather innocuous to monogastric species. Calcium sulfate and Mg sulfate are good sources of sulfate anion that may also supply Mg and Ca if needed. Sulfuric acid may also be used to increase diet sulfur to 4 g/kg DM if proper handling precautions are observed, which include a respirator as the fumes are very hazardous!

Now, with the exception of K and Cl, the “variables” in the various proposed DCAD equations have become “fixed”. The key to milk fever prevention (at least with Holstein cows) is to keep K as close to the NRC requirement of the dry cow as possible (about 10 g/kg DM). The key to reduction of subclinical hypocalcemia, not just milk fever, is to add Cl to the ration to counteract the effects of even low diet K on blood alkalinity. For formulation purposes the concentration of Cl required in the diet to acidify the cow is approximately 5 g/kg DM, less than the concentration of K in the diet. In other words, if diet K can be reduced to 13 g/kg DM, the Cl concentration of the diet should be increased to 8 g/kg/DM. If dietary K can only be reduced to 20 g/kg DM the diet Cl would need to be roughly 15 g/kg DM to acidify the cow. This level of Cl in the diet is likely to cause a decrease in dry matter intake. Chloride sources differ in their palatability and since achieving low dietary K can be difficult it is prudent to use a palatable source of Cl when formulating the diet. Ammonium chloride (or ammonium sulfate) can be particularly unpalatable when included in rations with a high pH. At the higher pH of some rations the ammonium cation is converted to

ammonia, which is highly irritating when smelled by the cow. Prilling the Cl (and SO_4) salts can reduce the unpleasant taste of the salts. In our experience, hydrochloric acid has proved the most palatable source of anions. As with sulfuric acid, hydrochloric acid can be extremely dangerous to handle when it is procured as a liquid concentrate. Several North American companies now manufacture hydrochloric acid based anion supplements, which are safe to handle.

These are simply guidelines for anion supplementation used by this author and are based on inclusion of Ca, Na, S, Mg, and P at the levels outlined above. Urine pH of the cows provides a cheap and fairly accurate assessment of blood pH and can be a good gauge of the appropriate level of anion supplementation (Jardon, 1995). Urine pH on high cation diets is generally above 8.2. Limiting dietary cations will reduce urine pH only a small amount (down to 7.8). For optimal control of subclinical hypocalcemia the average pH of the urine of Holstein cows should be between 6.2 and 6.8, which essentially requires addition of anions to the ration. In Jersey cows the average urine pH of the close-up cows has to be reduced to between 5.8 and 6.3 for effective control of hypocalcemia. If the average urine pH is between 5.0 and 5.5, excessive anions have induced an uncompensated metabolic acidosis and the cows will suffer a decline in dry matter intake. Urine pH can be checked 48 or more hours after a ration change. Urine samples should be free of feces and made on midstream collections to avoid alkalinity from vaginal secretions. The best estimate of acid–base status appears to be from samples obtained 6–9 h after fresh feed is offered, but timing is less critical than adopting the habit of regularly checking urine pH of cows in the last week of gestation. Anion supplemented diets are generally fed for the last 3 weeks before calving, though the length of time these diets need to be fed to induce a compensated metabolic acidosis is no more than 4–5 days.

3.5. Agronomic considerations

Reducing K in the ration of the late gestation cow can present a problem. All plants must have access to a certain amount of K to obtain maximal growth. Corn is a warm season grass that tends to contain 11–15 g K/kg DM. It is difficult to find any other forage this low in K. Other warm season (prairie) grasses, tend to be low in K but they are also low in protein and digestibility. Legumes and cool season grasses will accumulate K within their tissues to concentrations that are well above that required for optimal growth of the plant if soil K is high. Optimal growth of alfalfa occurs when the plant K concentration is around 20–22 g/kg DM. By restricting K application to the soil it is possible to avoid luxury consumption of K by legumes and cool season grasses. Most producers are aware of the need to procure low K forages for inclusion in dry cow rations. However, they should also be aware that forages take up Cl from the soil and it is possible to find hays that are low K and high (10–12 g/kg DM) Cl. Producers should utilize the lowest DCAD forage possible, not simply the lowest K forage. A low DCAD forage is also not useful if it is unpalatable—highly mature forages, or those rained on during the drying process are low in K but tend to be less palatable. Producers should routinely analyze for both K and Cl in forages intended for dry cows in late gestation. Though Na is a cation that figures prominently in DCAD equations, forage Na rarely contributes significant mEq of cation to the diet.

If grasses and legumes contain less K than 20 g/kg DM it is likely the yield of hay has suffered. Most farms will still want to optimize yield—the threat arises from uncontrolled fertilization of hay crops intended for dry cows. (Lactating cows will actually perform better on the higher DCAD forages (Sanchez et al., 1994).) When liquid manure is applied to the land it brings large amounts of K to the soil and relatively small amounts of Cl. Forages become very high in DCAD. About 0.9 of potash used is KCl (muriate of potash). If potash is used to meet the K needs of the plants the DCAD may not be so severely high as the K ions taken up within the plant are often accompanied by Cl ions.

Although not yet well tested it is possible to fertilize land with chloride to produce high chloride forages. In a preliminary trial, 50 kg chloride/ha as calcium chloride was added to a portion of a grass/clover crop, which was later harvested as silage to be fed to the dry cows. The chloride content of the silage was increased from 6 to 15 g/kg DM. This did not seem to affect palatability of the forage. At a daily intake of 6 kg silage DM, this implied an increase on the dietary intake of anions of 1521 mEq, which might be a critical difference when trying to create a low DCAD diet (Pehrson et al., 1999). Unpublished studies in our lab and the lab of Ev Thomas at the Miner Research Institute, Chazy NY (personal communication) have confirmed similar responses in alfalfa and grass hays, and have not observed a decline in yield of forage with these treatments.

3.5.1. Ca deficient diet to stimulate PTH secretion pre-calving

When cows are fed a diet that supplies less Ca than they require, the cows are in negative Ca balance. This causes a minor decline in blood Ca concentration stimulating PTH secretion, which in turn stimulates osteoclastic bone resorption and renal production of 1,25-dihydroxyvitamin D. At parturition the cow's osteoclasts are already active and in high numbers and the lactational drain of Ca is more easily replaced from bone Ca. If provided with Ca in the lactation ration, the previous stimulation of enterocytes by 1,25-dihydroxyvitamin D will allow efficient utilization of dietary Ca and the cow avoids hypocalcemia (Goings et al., 1974; Green et al., 1981).

The 2000 NRC lists the Ca requirement of the cow in terms of absorbable Ca, since the availability of Ca in diets varies. The absorbable Ca requirement (NRC, 2000) of the late gestation cow is from 14 g/day in Jerseys to about 22 g in large Holsteins. A truly low Ca diet capable of stimulating PTH secretion supplies considerably less absorbable Ca than required by the cow (Goings et al., 1974; Green et al., 1981). A 600 kg cow consuming 13 kg DM must be fed a diet that is less than 1.5 g absorbable Ca/kg DM if it is to provide less than 20 g available Ca/day. Low Ca diets have proved more practical under grazing situations. In these cases, the total dry matter intake of pasture was 6–7 kg DM/day and the grasses being grazed were less than 4 g Ca/kg DM, which would provide <28 g total Ca and somewhere around 9–10 g absorbable Ca/day (Sanchez, 2003). It is important to note that after calving the animal is switched to a high Ca diet.

Recently, two methods have been developed to reduce the availability of dietary Ca for absorption. The first method involves incorporation of zeolite (a silicate particle) into the ration, which binds Ca and causes it to be passed out in the feces. At present, the method is unwieldy because very large amounts of zeolite must be ingested each day (0.5–1 kg/day for 2 weeks before calving) and the effects of zeolite on P and trace mineral absorption are not clear (Thilsing-Hansen et al., 2002, 2003). By chemically modifying the zeolite it is

theoretically possible to increase the affinity and the specificity of the zeolite for Ca, which may allow its practical use. The second method involves administration of vegetable oils, which bind Ca to form an insoluble soap preventing absorption of diet Ca (Wilson, 2003). These methods have been successfully used in cattle fed diets containing 30–50 g Ca/day. They irreversibly bind enough dietary Ca to cause the reaction typically seen when the diet provides <15 g absorbable Ca/day.

3.5.2. Vitamin D supplementation

A reasonable practice is to supplement the dry cow with 20–30,000 IU Vitamin D/day in the diet. Earlier literature often recommended feeding or injecting massive doses (up to 10 million units of Vitamin D) 10 days–2 weeks prior to calving to prevent milk fever (Hibbs and Conrad, 1976; Littledike and Horst, 1980). These Vitamin D doses pharmacologically increased intestinal Ca absorption, and sometimes prevented milk fever. Unfortunately the dose of Vitamin D that effectively prevented milk fever was very close to the dose causing irreversible metastatic calcification of soft tissues. Lower doses (500,000–1 million units of Vitamin D) actually induced milk fever in some cows because the high levels of 25-OH D and 1,25-dihydroxyvitamin D resulting from treatment suppressed PTH secretion and renal synthesis of endogenous 1,25-dihydroxyvitamin. These animals become hypocalcemic when the exogenous source of Vitamin D that had maintained elevated intestinal Ca absorption rates was cleared from the body. In some cases, the ability to begin endogenous production of 1,25-dihydroxyvitamin D was suppressed for a week after calving (Littledike and Horst, 1980).

Treatment with 1,25-dihydroxyvitamin D and its analogues can be more effective and much safer than using Vitamin D but problems associated with timing of administration remain (Bar et al., 1985; Goff et al., 1988). The problem of suppression of renal 1,25-dihydroxyvitamin D production can be minimized by slow withdrawal of the exogenous hormone over a period of days after calving (Goff and Horst, 1990).

3.5.3. Oral Ca treatments at calving

Ca administered to the fresh cow may arguably be called a treatment rather than a preventative measure for hypocalcemia. Contrasts between the effects observed with intravenous, subcutaneous, and oral Ca treatments have been described elsewhere (Goff, 1999). Briefly, the concept behind oral supplementation is that the cow's ability to utilize active transport of Ca across intestinal cells is inadequate to help her maintain normal blood Ca concentrations. By dosing the animal with large amounts of very soluble Ca it is possible to force Ca across the intestinal tract by means of passive diffusion between, not across, intestinal epithelial cells. Best results are obtained with doses of Ca between 50 and 125 g Ca/dose. Ca chloride has been used but can be caustic. Large or repeated doses of calcium chloride can induce an uncompensated metabolic acidosis in the cow, especially if the cow is already being fed an acidogenic diet (Goff and Horst, 1993). Ca propionate is less injurious to tissues and is not acidogenic. It has the added benefit of supplying propionate, a gluconeogenic precursor Goff and Horst, 1993; Pehrson et al., 1998). For best control of hypocalcemia a dose is given at calving and again 24 h later. Larger or more frequent dosing can be toxic. Toxic doses of Ca can be delivered orally—about 250 g Ca in a soluble form will kill some cows (Goff et al., 2002). The benefit of adding oral Ca on top of a properly formulated

low DCAD program does not seem to warrant the added expense (Melendez et al., 2002).

3.6. Magnesium

Mg is a major intracellular cation that is a necessary cofactor for enzymatic reactions vital to every major metabolic pathway. Extracellular Mg is vital to normal nerve conduction, muscle function, and bone mineral formation. Cow plasma Mg concentration is normally between 1.8 and 2.4 mg/dl (0.75 and 1.0 mmol/L). In a 500 kg cow there is about 0.7 g Mg in the blood, 2.5 g Mg in all extracellular fluids, 70 g Mg inside cells, and 170 g Mg within bone mineral (Mayland, 1988). Milk is approximately 5.2 mmol/L Mg and milk production in lactating animals can rapidly deplete extracellular Mg resulting in hypomagnesemia if not replaced. Bone is not a significant source of Mg that can be utilized in times of Mg deficit, as bone resorption occurs in response to Ca homeostasis, not Mg status. Maintenance of normal plasma Mg concentration is nearly totally dependent on a constant influx of Mg from the diet. Thus, inappetance in the cow is often accompanied by mild to moderate hypomagnesemia. Homeostasis also involves excretion of any excess magnesium via the kidneys.

Mg is well absorbed from the small intestine of young calves and lambs. As the rumen and reticulum develop these sites become the main, and perhaps the only, sites for net Mg absorption (Pfeffer et al., 1970; Martens and Rayssiguier, 1980; Martens and Gabel, 1986). In adult ruminants the small intestine becomes a site of net secretion of Mg (Greene et al., 1983).

Mg absorption from the rumen is dependent on the concentration of Mg in solution in the rumen fluid and the integrity of the Mg transport mechanism, which is a Na-linked active transport process (Martens and Gabel, 1986).

The soluble concentration of Mg in rumen fluid is obviously dependent on the magnesium content of the diet. However, Mg solubility declines sharply as rumen pH rises above 6.5. Forages often contain 100–200 mmol/kg of unsaturated palmitic, linoleic, and linolenic acids, which can form insoluble Mg salts in the rumen. Plants also can contain trans-aconitic acid. A metabolite of trans-aconitic acid, tricarballylate can complex Mg and is resistant to rumen degradation and may play a role in hypomagnesemic tetany (Cook et al., 1994).

3.7. Factors affecting the active transport mechanism for absorbing Mg across the rumen

Active transport of Mg across the rumen wall is a Na-linked transport process. Forages and pastures are generally fairly low in Na. Adding Na to the ration can improve Mg transport across the rumen when dietary Na is low, though in high amounts it increases urinary excretion of Mg so that the benefit to the animal may be negated. High dietary K can reduce the absorption of Mg (Schonewille et al., 1992). Newton et al. (1972) fed lambs either a low K diet (6 g K/kg DM) or high K diet (49 g/kg DM) and found about a 0.5 reduction in apparent Mg absorption. High K concentration in the rumen fluid depolarizes the apical membrane of the rumen epithelium reducing the electromotive potential needed to drive Mg across the rumen wall (Martens and Kasebieter, 1983). The negative effects of a high K diet cannot be overcome by adding extra Na to the diet (Martens et al., 1988). Feeding

ionophores (monensin, lasalocid) can improve activity of the Na-linked Mg transport system in the rumen, increasing Mg absorption efficiency about 0.1 (Greene et al., 1986). However, ionophores are not approved for use in many of the animals they could benefit.

3.8. Utilizing other transport mechanisms to absorb dietary Mg

The active transport mechanism for Mg absorption across the rumen wall is critical to the survival of the animal when dietary Mg concentration is less than 2.5 g/kg DM. Unfortunately there are several known factors, such as dietary K, and several unknown factors that prevent efficient Mg absorption by this pathway. A second pathway for absorption of Mg exists which operates only at high rumen fluid Mg concentrations. At high rumen Mg concentration the Mg will flow down its concentration gradient into the extracellular fluids of the cow (Martens and Schweigel, 2000). This passive transport mechanism is not subject to poisoning by K and is only subject to the concentration of soluble Mg in the rumen.

The concentration of Mg in rumen fluid needed to utilize concentration gradient driven absorption of Mg is greater than 4 mmol/L (Care et al., 1984; Ram et al., 1998). The minimum level of Mg required in the diet to prevent negative Mg balance in the face of high K levels in ruminants is approximately 3.5 g/kg DM (Ram et al., 1998). Mg content of the close-up dry cow ration and the early lactation ration should be between 3.5 and 4 g/kg DM as insurance against the possibility that the active transport processes for Mg absorption are impaired.

3.9. Mg status

Ordinarily any dietary Mg that is absorbed and is not required for maintenance and growth of tissues, fetal development, or lactation, is excreted by the kidneys. Most of the Mg filtered across the renal glomeruli is reabsorbed by the renal tubular epithelium. At a certain blood Mg level the amount of Mg filtered across the glomerulus exceeds the capacity of the renal tubules to reabsorb the filtered Mg. This point is considered the renal threshold for Mg. In cattle, the renal threshold is exceeded when blood Mg exceeds about 0.74 mmol/L (Littledike and Goff, 1987). However, PTH can cause increased renal tubular reabsorption of Mg—increasing the renal threshold for Mg. The kidneys excrete less Mg and this causes blood Mg to be elevated. This is the typical scenario in a milk fever cow that has received adequate Mg in her ration (Goff et al., 1989). However, if dietary Mg is insufficient or rumen absorption of Mg is impaired there is not enough blood Mg absorbed to even reach the normal renal threshold for Mg. Sampling the blood of several cows within 12 h after calving is an effective index of Mg status of the periparturient cows. If serum Mg concentration is not at least 0.8 mmol/L it suggests inadequate dietary Mg absorption and that hypomagnesemia may be limiting productivity as well as contributing to hypocalcemia in the herd. Less than 0.87 mmol/L Mg will appear in the urine of a cow that is hypomagnesemic. A cow receiving adequate diet Mg will generally have more than 4.3 mmol/L Mg in her urine (Puls, 1994). Often residual urine can be found in the bladder of a dead cow, which may allow diagnosis of grass tetany in cattle found dead at pasture. While clinical signs of grass tetany are obvious—recumbency, convulsions, nystagmus; these symptoms are only observed when blood Mg falls below 0.4–0.5 mmol/L. Grass tetany is often accompanied by

severe hypocalcemia. Cows with blood Mg between 0.5 and 0.8 mmol/L have few obvious clinical symptoms—they are slow to eat and are not producing milk up to their potential. Response to an increase in dietary Mg is generally rapid (weeks) and includes an increase in milk production.

3.10. Phosphorus

Traditionally, Phosphorus in clinical medicine is abbreviated as P, although it should be understood by the reader that the biologically relevant form of P is actually inorganic phosphate, not elemental phosphorus. P is a component of phospholipids, phosphoproteins, nucleic acids, and energy transferring molecules such as ATP. P is an essential component of the acid–base buffer system. It is second only to Ca as a major component of bone mineral.

Plasma P concentration is normally 1.3–2.6 mmol/L. Maintaining the extracellular P pool involves replacing P removed for bone and muscle growth, endogenous fecal loss, urinary P loss, and milk production with P absorbed from the diet or resorbed from bone (Reinhardt et al., 1988). During late gestation fetal skeletal development can withdraw up to 10 g P/day from the maternal P pools (House and Bell, 1993). About 0.3 g P is incorporated into each kg of body tissue (muscle) gained during growth of the animal (ARC, 1980; Bacon et al., 1990). Production of milk removes about 1 g P from the extracellular pool/kg of milk produced. Salivary glands remove between 30 and 90 g P from the extracellular P pool each day, which is a major buffer of rumen pH—most of this secreted P is reabsorbed in the small intestine to return to the extracellular pool.

Rumen microbes are able to digest phytic acid so that most of the phytate-bound P, the form of 0.35 and 0.70 of P in plants, is available for absorption in ruminants. P is primarily absorbed in the small intestine via an active transport process that is responsive to 1,25-dihydroxyvitamin D. Intestinal P absorption efficiency can, in theory, be upregulated during periods of P deficiency as renal production of 1,25-dihydroxyvitamin D is directly stimulated by very low plasma P. However, the plasma P level must reach very low levels (0.3–0.6 mmol/L) to actually stimulate increased renal production of 1,25-dihydroxyvitamin D. Plasma P concentrations are generally well correlated with dietary P absorption. P absorbed in excess of needs is excreted in urine and saliva.

PTH, secreted during periods of Ca stress, increases renal and salivary excretion of P (Wright et al., 1984), which may be detrimental to maintenance of normal blood P concentrations. This is the likely reason that hypocalcemic animals tend to become hypophosphatemic. One might believe that prolonged PTH secretion would increase blood P concentration since it stimulates bone mineral resorption, but this effect is small when compared too the effect of PTH on P excretion. Since PTH stimulates the kidney to produce 1,25-dihydroxyvitamin D, it eventually can increase the efficiency of intestinal phosphate absorption, which should correct hypophosphatemia. However, it must be remembered that PTH is secreted in response to hypocalcemia, not hypophosphatemia.

3.11. Hypophosphatemia and downer cows

In late gestation plasma P can decline precipitously as the growth of the fetus accelerates and removes substantial amounts of P from the maternal circulation. These animals often

become recumbent and are unable to rise, though they appear fairly alert and will often eat feed placed in front of them. Cows carrying twins are most often affected. Plasma P concentration in these recumbent animals is often less than 0.3 mmol/L. The disease is usually complicated by concurrent hypocalcemia, hypomagnesemia, and in some cases hypoglycemia. Diets that are marginal in P are generally indicative of diets that are marginal in energy, since grains are usually very good sources of P.

At the onset of lactation the production of colostrum and milk draws large amounts of P out of the extracellular P pools. This alone will often cause an acute decline in plasma P levels. In addition, if the animal is also developing hypocalcemia, PTH will be secreted in large amounts, increasing urinary and salivary loss of P. In dairy cows, plasma P concentrations routinely fall below the normal range at parturition and in cows with milk fever plasma P concentrations are often between 0.4 and 0.8 mmol/L. Plasma P concentrations usually increase rapidly following treatment of the hypocalcemic cow with intravenous Ca solutions. This rapid recovery is due to reduction in PTH secretion, which reduces urinary and salivary loss of P. Administration of Ca generally causes resumption of gastrointestinal motility, which allows absorption of dietary P and reabsorption of salivary P secretions (Goff, 1998).

Some dairy cows developing acute hypophosphatemia do not spontaneously recover normal plasma P concentration. This is the case in some cows that are classified as “downer cows”. The term downer cow is used for any cow that is unable to rise to her feet, whether the cause be a mineral imbalance, ruptured tendons or nerve damage, or an illness such as endotoxemia. Hypophosphatemic downer cows are also often described as “alert” downers. That is they are curious and move their head when approached. They will often eat feed placed before them. They sometimes crawl, but are incapable of getting to their feet. This syndrome often begins as milk fever but unlike the typical milk fever cow, plasma P remains low (below 0.3 mmol/L in most of these cows) despite successful treatment of the hypocalcemia. While clinical cases of this syndrome have been difficult to study it has been our experience that protracted hypophosphatemia in these cows appears to be an important factor in the inability of these animals to rise to their feet, but why plasma P remains low is unclear. In some cases, the inability to absorb the salivary phosphate may be secondary to poor rumen motility, but this is not a feature found in all cases. Excessive cortisol secretion could also drive blood P concentration down, probably by forcing extracellular P inside cells (Horst, 1976). Treatment of cows with phosphate containing solutions can affect recovery in some animals. For oral treatment the dose is 50 g P supplied in a 200 g monosodium phosphate drench. Intravenous treatment consists of 6 g P supplied by 23 g monosodium phosphate dissolved in 1 l of saline. Oral treatment restores normal blood P more slowly than intravenous treatment but the effect lasts much longer (Cheng et al., 1998). If depletion of intracellular P stores is also involved in the downer syndrome, it seems likely that intravenous treatment alone simply does not supply enough P to replenish intracellular stores of P.

The hypophosphatemic downer cow syndrome does not appear to be caused by low P diets as affected cows are often receiving diets containing at least 4 g P/kg DM. Most of the cases are reported in northern climates in winter, so there may be some effect of cold exposure (stress??) on phosphorus metabolism. The best preventative measure is to avoid development of hypocalcemia since most cases appear to be secondary to milk fever.

Many cows will have moderate hypophosphatemia, with a blood P concentration between 0.8 and 1.1 mmol/L, for the first few days of lactation. While we speculate that this may be detrimental to feed intake and digestion and perhaps is sub-optimal for other P functions in the body, there are no studies in the literature to support or oppose this view. Most of these cows will rapidly restore blood P concentrations to normal levels if they are consuming feed. Hypophosphatemia is also implicated as the cause of post-parturient hemoglobinuria. There is some evidence that prolonged (more than 2 weeks) hypophosphatemia interferes with glycolysis and ATP formation in the red blood cells. The lack of ATP increases the fragility of the red blood cells leading to lysis and hemoglobinuria. Often ketosis, copper and/or selenium deficiency, and poor anti-oxidant status are factors that, along with hypophosphatemia, precipitate post-parturient hemoglobinuria (Chugh et al., 1998; Wang et al., 1985; Jubb et al., 1990).

3.12. Potassium

Metabolism of K in cows is poorly researched since most diets provide more than ample supplies of K to the cow. However, severe hypokalemia occasionally develops which has been associated with muscle weakness and recumbency in cows. Most reports have been retrospective studies of clinical cases presented to veterinary colleges. The majority of cases present with severe hypokalemia (plasma K below 2.5 mmol/L) and most cases occur secondary to prolonged inappetance, often secondary to other illnesses. Ketosis is commonly the factor precipitating the inappetance.

Extracellular K concentration is normally 3.9–5.8 mmol/L and plays a vital role in osmotic equilibrium, and maintenance of acid–base balance. Intracellular K concentration is 150–160 mmol/L. Intracellular K is a co-factor of enzymes involved in protein synthesis and carbohydrate metabolism, and K plays a major role in intracellular osmotic and acid–base equilibrium. The ratio of intracellular:extracellular fluid K concentration is the main determinant of resting cell membrane potentials, which affects nerve and muscle cell excitability.

K can move between extracellular and intracellular fluid compartments. Unfortunately this movement is not always very predictable, a normal blood K concentration may not indicate normal intracellular stores of K, and abnormal blood K concentration does not necessarily indicate abnormal store or concentration of K inside cells.

3.13. Effects of K on muscle function

K is the major determinant of nerve and muscle cell resting membrane potential since the majority of ion channels that are open in the resting cell membrane are K channels. Therefore, variations in the K concentration gradient will have large effects on resting membrane potential which can be calculated using the Nernst equation (at 37 °C):

$$\text{Membrane potential (mV)} = 61.5 \times \log([K_i]/[K_o]),$$

where K_i is the K concentration inside the cell and K_o is the K concentration outside the cell. For example, under normal conditions when K_i = 150 mmol/L and K_o = 4 mmol/L, the concentration ratio is 38:1 (150/4 mmol/L) and the predicted membrane potential is −97 mV.

A small decline in extracellular K concentration will have a dramatic effect on the cell resting membrane potential. If plasma K falls to 2 mmol/L the ratio becomes 75:1 (150/2 mmol/L) and the predicted membrane potential increases to −115 mV, making the cell much less likely to reach the threshold potential which will trigger an action potential. An increase in plasma K to 6 mmol/L decreases the K_i/K_o ratio to 25:1 and the resting membrane potential becomes −86 mV; closer to the threshold for opening the Na channels in the cell to initiate an action potential. Cardiac muscle reacts differently. Hypokalemia generally causes a loss of K conductance in cardiac muscle depolarizing cardiac cell membranes (Schipperheyn, 1984).

If an action potential is somehow successfully propagated down a motor nerve, hypokalemia, because it hyperpolarizes the resting cell membrane, will reduce the amount of acetylcholine released by the nerve ending at the motor end plate. This reduces the number of muscle fibers likely to contract causing muscle weakness (Katz, 1962).

Intracellular K concentration plays a role in the conformation of Ca channels that regulate release of Ca from the sarcoplasmic reticulum in response to a membrane potential. Depletion of intracellular K reduces Ca release, which prevents effective interaction of actin and myosin molecules and reduced contractility of muscle (Meissner et al., 1997).

3.14. Metabolism

Normal bovine plasma K concentration is about 3.9–5.8 mmol/L. Cattle ordinarily consume diets that contain more than enough K to meet their tissue requirements (NRC, 2000). Since nearly all of the dietary K is absorbed across the intestinal tract preventing an excessive increase in plasma K is a daily reality. The kidneys are expected to excrete any excess absorbed K. Renal K excretion is controlled by aldosterone, which enhances renal secretion of K in exchange for Na ions. High blood K concentration (hyperkalemia) can directly stimulate secretion of aldosterone by the adrenal glands. However, low plasma Na and low plasma volume are more potent triggers for aldosterone secretion. Since low plasma volume is the most potent stimulant of aldosterone secretion it is possible to have scenarios where hypokalemia develops secondary to low plasma Na and low plasma volume. Aldosterone can also increase gastrointestinal secretion of K within saliva and pancreatic secretions, which can aid the kidneys in preventing hyperkalemia. It is important to point out that dietary K can enter the extracellular fluids very rapidly following a meal, while the kidney will take several hours to excrete the excess K. Another mechanism is needed to prevent hyperkalemia following a meal. This mechanism involves shifting K from extracellular to intracellular fluids. Intracellular uptake of K is mediated primarily by insulin secreted in response to elevated plasma K concentration (and also in response to hyperglycemia). Insulin increases the activity of the Na–K ATPase pump, particularly in the liver and skeletal muscle, increasing uptake of K by these tissues. Beta 2-adrenergic catecholamines (*i.e.* epinephrine) can also drive K intracellularly. Epinephrine probably protects the animal from hyperkalemia during and following exercise. During exercise K is lost from muscle during excitation–contraction of muscle. Stimulation of B2-catecholamine receptors stimulates Na–K ATPase to reduce extracellular K by driving K into muscle and liver.

Another confounding problem in understanding K metabolism is its subservient relationship with acid–base balance. Because disturbances in acid–base balance are debilitating or

lethal, the maintenance of a stable pH of the extracellular fluids is of paramount importance. When H^+ concentration begins to rise in the blood of the cow, K will leave the intracellular fluids and enter the extracellular fluids. At the same time the intracellular fluid gains H^+. Hyperkalemia often is the result of the body's attempt to combat acidosis. Conversely, if the animal is at risk of developing alkalosis, K^+ leave the extracellular fluids causing hypokalemia, intracellular H^+ levels decrease, and extracellular H^+ concentrations increase to restore normal blood pH.

Because dietary K is usually more than adequate there is not an elaborate mechanism developed to avoid hypokalemia. Under most conditions hypokalemia is corrected by simply reducing aldosterone secretion. So long as the cow is eating, hypokalemia is generally easily avoided. However, if the cow is not eating, hypokalemia could quickly ensue, as illustrated by examining K balance in the cow.

3.15. K Balance in the cow

In a 600 kg cow there will be approximately 1150 g K within the cells of the body and about 23 g K in all the extracellular fluids, with about 7 g K in the plasma pool. The maintenance requirement for K is the sum of the endogenous urinary K loss (amount of K lost in urine when cows are on a K deficient diet, which is about 0.038 g K/kg body wt.) plus endogenous fecal losses (approximately 6.1 g K is lost/kg dry matter ingested) (NRC, 2000). Milk contains approximately 1.5 g K/kg and fetal development in late gestation requires about 1 g K/day.

If this cow is in very early lactation and ingesting 14 kg DM/day, her maintenance requirement is about 108 g K/day. If her diet is 15 g K/kg DM, we can assume she is ingesting 210 g K/day and about 189 g K is absorbed. If she is producing 15 kg milk the first day of lactation, she will utilize 22.5 g K for milk production. Of the 189 g K entering her body, 108 g K is used for maintenance and 22.5 g K is utilized for milk. This leaves 58.5 g excess K to be excreted in the urine if she is to avoid hyperkalemia.

What if this cow suddenly goes off feed due to some secondary illness? K balance calculations would suggest this cow would rapidly go into negative K balance. Milk production would continue to withdraw 22.5 g K/day and the obligatory urinary K loss would be about 22 g/day for a net loss of 44.5 g K. There is some lag time between the cessation of aldosterone secretion and the cessation of K secretion by the kidneys so the urinary loss may initially be higher than the obligatory K loss in urine. Considering that there is only about 23 g K in all the extracellular fluids the cow should develop hypokalemia.

However, simply fasting a cow does not constitute enough of a challenge to K metabolism to cause the severe hypokalemia associated with the downer cow syndrome. Holstein non-pregnant, non-lactating, cows fasted for 48 h had a decline in plasma K from 4.9 to 4.3 mmol/L (Clabough and Swanson, 1989). Plasma K of beef steers fasted for up to 4 days fell from 4.1 to 3.7 mmol/L (Smith and Prior, 1984). Larger declines in blood K due to fasting are prevented by K that enters the plasma pool from muscle. Hypokalemia alone can trigger a reduction in Na–K ATPase activity in muscle. Reducing pump activity does not allow the muscle to replace K that chronically leaks from the muscle cell, especially during excitation of the muscle. Intracellular K concentration eventually falls, and intracellular Na concentration increases (Thompson and McDonough, 1996). This response is unique

to muscle–liver and other tissue intracellular K concentration does not decrease during hypokalemia (McDonough et al., 2002).

3.16. Hypokalemia and "downer cows"

As a general rule, K homeostasis will effectively prevent severe hypokalemia, if the animal is only off feed for a few days (before muscle is severely depleted of K). Hypokalemia, as a cause of the downer cow syndrome, is rather uncommon and the cases that do occur often are caused by human intervention as explained below. In most reports concerning clinical cases of hypokalemia and recumbency in cows the plasma K concentration is less than 2.5 mmol/L (Sielman et al., 1997; Sattler et al., 1998; Peek et al., 2003). In many of the affected cows plasma K concentration is less than 1.8 mmol/L. The degree of hypokalemia observed simply from inappetance of just 4–5 days is unlikely to be severe enough to cause flaccid paralysis in the cow. The severely hypokalemic cow tends to be very depressed. Though inappetance will greatly reduce the amount of K entering extracellular pools some other factor must also be causing depletion of extracellular and intracellular K.

The possibilities causing low plasma K include exaggerated renal excretion of K and excessive uptake of K by cells. The possibilities causing intracellular K depletion include prolonged fasting and exaggerated renal excretion of K.

3.17. Factors exaggerating renal K secretion

Excessive aldosterone secretion by the adrenal gland is relatively rare in cattle. However, drugs with glucocorticoid activity are often administered to cattle in early lactation as anti-inflammatory agents or to stimulate gluconeogenesis in cows exhibiting ketosis. If those drugs also have mineralocorticoid activity they will stimulate urinary K secretion. In the inappetant cow the muscles are releasing K to support normokalemia. If this K is being rapidly excreted by the kidney the muscle K pool will be quickly depleted and severe hypokalemia can ensue. Isoflupredone acetate is administered to cows for its glucocorticoid activity but it has enough mineralocorticoid activity to enhance renal K secretion and administration of this steroid has been implicated as a factor causing severe hypokalemia in cows. Usually affected cows have been repeatedly injected with isoflupredone acetate prior to the onset of recumbency (Sielman et al., 1997; Peek et al., 2003).

3.18. Treatment

Intravenous treatment is necessarily slow (to avoid hyperkalemia and heart stoppage) and should be limited to 0.5 mEq/kg/h (Sweeney, 1999). Oral therapy with KCl has proven a more effective therapy as enough K can be delivered to replace intracellular as well as extracellular K. It is also less expensive. Oral treatment consists of the administration of KCl at 100–150 g/dose given twice/day in several gallons of water for several days. Concommittant treatment with oral glucose precursors or intravenous dextrose to cause an insulin surge can help drive the absorbed K into the cells, and will help treat the underlying ketosis present in most affected cows.

If dehydration is present, plasma volume needs to be corrected first. Dehydration will cause aldosterone secretion and much of the K absorbed across the intestine will be excreted in the urine without restoring intracellular pools. Re-hydration will also help the cow restore normal acid–base balance.

Severe hypokalemia resulting in the down cow is a relatively rare phenomena. Although intracellular stores of K have not been measured in affected cows the course of the disease and the poor response to intravenous K therapy alone suggest muscle depletion of K is a primary component of the disorder. In the majority of reported cases the administration of steroids that have substantial mineralocorticoid activity is largely responsible for the severe K depletion observed. Overzealous use of exogenous insulin or intravenous glucose administration may also be a factor causing these severe declines in plasma K in inappetant cows.

Moderate hypokalemia does not cause the flaccid paralysis associated with the hypokalemic downer cow syndrome. Moderate hypokalemia is common in anorexic cattle and severe hypokalemia is prevented by the release of K from intracellular stores in muscle and liver.

If severe depletion of muscle K causes severe loss of muscle function and down cows, does moderate loss of K from muscle cause sluggish behavior in cows? The fresh cow often is faced with metabolic or infectious disease challenges that cause various degrees of anorexia and moderate hypokalemia. Would aggressive treatment of anorexic cows with oral KCl allow better muscle function in these cows, giving them the strength to fight at feed bunks, and restore them to productivity sooner?

4. Summary

Every cow is likely to develop mild hypocalcemia, hypokalemia, and hypophosphatemia within a day or two of calving. A mild perturbation of blood calcium serves as the trigger to initiate calcium homeostatic mechanisms by the body. When diet cation–anion difference is favorable this perturbation in blood calcium is rapidly and successfully overcome, independent of diet calcium content. When DCAD is unfavorable, the cow is at greater risk of developing more severe hypocalcemia and milk fever. Adjusting DCAD can be difficult and requires a concerted agronomic effort on the farm. In some cases a more practical option is to devise a very low calcium diet to be fed prior to calving to stimulate calcium homeostasis, prior to calving—to prime the animal to the impending calcium drain. While it is true that very low calcium diets can be used to prevent milk fever it must be remembered that it is not true that higher calcium diets cause milk fever. Mild hypokalemia will occur in most dairy cows as they generally suffer a reduction in feed intake in early lactation, and they begin to produce milk rich in potassium. It is interesting to keep in mind that the potassium content of milk is greater than the calcium content of milk, though it is well understood that the high calcium content of milk is the factor causing a drain on blood calcium concentration. Very rarely the animal develops severe hypokalemia, the reasons for this are complicated, but it appears that both intracellular and extracellular potassium pools are depleted in these animals, which causes the flaccid paralysis typical of the recumbent hypokalemic cow. Feeding higher potassium diets is not the preventative for this syndrome! Avoiding inappetance

is the key to prevention of this syndrome. Mild hypophosphatemia occurs secondary to hypocalcemia as the parathyroid hormone secreted in response to hypocalcemia affects phosphorus metabolism. Parathyroid hormone increases phosphate secretion in saliva and to a lesser extent the kidneys. Rumen stasis around the time of calving can trap the phosphate in the rumen, rather than allowing it to be passed into the intestine where it can be reabsorbed to restore blood phosphorus. Feeding higher phosphorus diets does not prevent this syndrome. Hypomagnesemia, or blood magnesium less than 0.83 mmol/L, should not occur in the periparturient dairy cow! When it does it signifies inadequate dietary magnesium absorption. Hypomagnesemia is another factor that can cause hypocalcemia in dairy cows. Hypomagnesemia reduces parathyroid hormone secretion in response to hypocalcemia and also interferes with bone and kidney responsiveness to parathyroid hormone. Hypomagnesemia is very amenable to prevention by increasing dietary magnesium content and form.

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